



दिल्ली DELHI

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PATENT
2761-0169P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Naveen ARORA et al. Conf.: 3751
 Appl. No.: 10/715,482 *Nov 19* Art Unit: 1645
 Filed: November 19, 2003 Examiner: Ford, V.L.
 For: A NOVEL PROTEIN CAPABLE OF INHIBITING ANTHRAX
 TOXIN ACTIVITY

DECLARATION UNDER 37 C.F.R. § 1.132

Honorable Commissioner of Patents
 Washington, D.C. 20231

Sir:

Naveen
 I, Naveen Arora hereby declare as follows:

1. I am a citizen of India, residing at G 110, Ashok Vihar, Phase 1, Delhi 110052, India.
2. I am presently employed as Scientist at Institute of Genomics and Integrative Biology, CSIR, Mall Road, Delhi 110007, India. A copy of my Curriculum Vitae is attached as Annexure 1.

BEST AVAILABLE COPY

3. I am a co-inventor of the subject matter of the above-identified U.S. Patent application 10/715482. I am familiar with the specification and pending claims, and with the prosecution history of the application.

4. The Examiner has rejected claims 1-8 and 21 as lacking novelty over Verma et al., *International Archives of Allergy and Immunology* 122:251-256 (2000). The Examiner asserts that a 67 kDa protein described in the paper as purified to homogeneity from a pollen extract of *Imperata cylindrica* is identical to the protein of the present invention as described in claims 1-8 and 21.

5. The purification performed by Verma et al. is described at page 252 of the reference, under the headings of "Pollen Extraction", "Ion Exchange Column Chromatography", "Gel Filtration Column Chromatography" and "Fast Protein Liquid Chromatography" (FPLC). It should be noted that the pollen extract was subjected to gel filtration chromatography followed by two different protocols of ion exchange chromatography.

6. The purification results of Verma et al. are described in Figure 1 and in the text, especially at pp. 253-255 of the reference. Of particular interest is the conclusion stated at the top of the second column of p. 255, "[N]-terminal amino acid was analyzed by Edman's degradation technique and found to be blocked."

7. On the other hand, the protein of the present invention was prepared as described in Examples 2-4 of the instant specification (see, pp. 11-12). Briefly, pollen was de-fatted by extraction three times with diethyl ether, followed by aqueous extraction with phosphate buffered saline. The pollen extract was then subjected to High Performance Liquid Chromatography on a "reverse phase" hydrophobic interaction medium (octadecyl silica). The 67 kDa protein of the invention was obtained as a homogeneous fraction by this single purification step. See, Figure 1(b), fractions 40, 50 and 60.

8. The pooled HPLC fraction of protein was subjected to amino-terminal sequencing by Edman degradation. The sequence D-[QT]-P-Y-S-E-K was obtained.

9. The obtaining of amino-terminal sequence data by Edman degradation of the protein purified as described in the instant specification, in comparison with the failure to obtain any sequence data due to blockage of the amino-terminus of the protein described by Verma et al. establishes

that these two proteins are distinct, and thus that the protein as claimed in the present invention is novel compared to the protein described by Verma et al. The conclusion that the protein of Verma et al. is distinct from the protein of the present invention is also consistent with the fact that different approaches to their purifications were used.

10. We further declare that blocking of the N-terminal of the protein disclosed in Verma et al 2000 did not occur during protein purification as they have purified the protein on ion exchange column using salt gradient. These conditions can not result in blocking of the amino group at the N-terminus.

11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: _____

By Naveen Arora
(name of Declarant) (NAVEEN ARORA)

ANNEXURE 1**CURRICULUM VITAE**

Name: Naveen Arora
Date & Place of Birth: 3rd January 1962, Delhi, INDIA
Citizenship: Indian
Marital Status: Married with 2 children
Addresses:
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 Room 509, Mall Road (near Jubilee Hall)
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Educational qualifications

July 1980-June 1983 B.Sc. (H) Chemistry, Univ. of Delhi, Delhi, India
 July 1983-June 1985 M.Sc. Biochemistry, Univ. of Delhi, Delhi, India
 July 1985-Sept. 1989 Ph.D. Medical Biochemistry, University of Delhi,
 Delhi, India

*Thesis Title: *Studies on Modified Allergens*

Professional/Research Experience:

July 2000 - Present **Scientist EI**, Institute of Genomics & integrative Biology,
 Delhi
 July 1995- July 2000 **Scientist C**, Centre for Biochemical Technology,
 Delhi 110007.
 Sept. 1992-June 1995 **Visiting Associate**, NIH, NIDR, Bethesda, MD20892, USA.
 Feb.1991-Sept. 1992 **Visiting fellow**, NIH, NIDR, Bethesda, MD 20892, USA.
 Sept. 1989-Jan.1991. **Visiting fellow**, NIH, NIAID, Bethesda, MD 20892, USA.
 July 1987-Aug. 1989 **Senior research fellow**, CSIR-CFB, Delhi 110007, INDIA.
 July 1985-July 1987 **Junior research fellow**, CSIR-CFB, Delhi 110007, INDIA.
 April 1984-July 1984 **Summer trainee**, CSIR-CFB, Delhi 110007, INDIA.

Membership of academic bodies

Fellow, Indian college of Allergy and Applied Immunology.
 Life member, Society of Biological Chemists (India).
 Life member, Indian Immunological Society.
 Life member, Indian Association of Microbiology
 Executive & Life member, Biotechnology Society of India
 Life member, Association of Clinical Biochemists of India

Awards and Honors

Alexander von Humboldt Fellowship	2002
Member, ICMR delegation visiting Germany on Hepatitis Workshop	2001
Goyal Young Scientist award	2000
Pharmacia Allergy Research Foundation Award	1997
M. Sundaramma Young Scientist oration lecture award	1996
Awarded a distinguished letter for performing excellent work in field of Allergy by NIAID, NIH, MD USA	1990
Young Scientist Award XVI Int. Cong. Allergy Appl. Immunol.	1988

Foreign Visits

Freiburg University Hospital, Germany	June –Nov. 2003
Freiburg University Hospital, Germany	June –Nov. 2002
Freiburg University, Germany	June 2001
Visiting Scientist Univ. Southern Calif., LA, USA	June-July 2000
Visiting Scientist Univ. Southern Calif., LA, USA	May-July 1998
Visiting Scientist Univ. Southern Calif., LA, USA	July-Oct. 1997

R & D Program Pursued/ current:**Ongoing Projects**

1. Development of protocols for allergenicity evaluation of Genetically modified foods. (DBT sponsored 2003-2006).
2. Task Force project on Asthma and Allergy Mitigation (CSIR sponsored, 2003- 2008)
3. Clinico-immunologic studies on allergen specific immunotherapy in patients of respiratory allergy (DST sponsored, 2004-2007).

Completed

1. Food as sensitizing agents in respiratory allergic disorders with special reference to bronchial asthma. (ICMR sponsored, 2002-2005).
2. Cloning, expression and immuno-chemical characterization of allergens by recombinant DNA methodology for use in diagnosis and immunotherapy of respiratory allergy diseases, Principal Investigator (DBT DO number BT/PRO/235/med/9/48/96, 1998-2001)
3. Development of Technology and Production of IL-2 and IL-10 by Recombinant Methods Principal Investigator (DBT DO number BT/12/05/96-PID, 1996-1999).

Teaching assignments

1. B. R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi, India
2. Faculty of Medical Sciences, University of Delhi, Delhi, India
3. Dept of Biotechnology and Biochemistry, Jiwaji University, Gwalior, MP, India

Publications

1. **Arora N.** and Gangal S.V. (1987): Studies on polymerized *Artemisia scoparia*: Preparation and immunologic response. Ind. J. Allergy Appl. Immunol., 1, 20-28.
2. Jaggi K. S., **Arora N.**, Niphadkar P.V. and Gangal S.V. (1983): Immunochemical

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- characterization of *Cocos nucifera* pollen. J. Allergy Clin. Immunol., **84**, 378-85.
3. **Arora N. and Gangal S.V. (1990):** Entrapment of allergen in liposomes reduces allergenicity and improves immunogenicity in preimmunized mice. Int. Arch. Allergy Appl. Immunol., **91**, 22-29.
 5. **Arora N. and Gangal S.V. (1990):** Immunomodulation by liposome entrapped allergen. Mol. Cellular Biochem. **97**, 173-179.
 6. **Arora N. and Gangal S.V. (1991):** Liposome as vehicle for allergen presentation in the immunotherapy of allergic diseases. Allergy **46**, 386-392.
 6. **Arora N. and Gangal S.V. (1992):** Efficacy of liposome entrapped allergen in regulation of IgE response in mice. Clin. Exp. Allergy, **22**, 35-42.
 7. **Arora N., Klimpel K.R., Singh Y. and Leppla S.H. (1992):** Fusions of anthrax toxin lethal factor to the ADP-ribosylation domain of *Pseudomonas* exotoxin A are potent cytotoxins which are translocated to the cytosol of mammalian cells. J. Biol. Chem. **267**, 15542-15548.
 8. **Mican J.A., Arora N., Burd P.R. and Metcalfe D.D. (1992):** Passive cutaneous anaphylaxis in mouse skin is associated with local accumulation of IL-6 mRNA and immunoreactive IL-6. J. Allergy Clin. Immunol. **90**, 815-824.
 9. **Arora N. and Leppla S.H. (1992)** Potent hybrid cytotoxins of anthrax toxin lethal factor and the ADP-ribosylation domain of *Pseudomonas* exotoxin A are translocated directly to the cytosol of mammalian cells. *Pseudomonas* News Lett. **17**, 2.
 10. **Sridhara S., Singh B.P., Arora N., Verma J. and Gangal S.V. (1992):** A study on antigenic changes during storage in three different biological extracts. Asian Pacific J. Allergy Immunol., **10**, 33-38.
 11. **Singh B.P., Sridhara S., Arora N. and Gangal S.V. (1992):** Evaluation of protein assay methods to identify their suitability for various pollen and fungal allergen extracts. Biochem. Internat., **27**, 477-484.
 12. **Arora N. and Leppla S.H. (1993):** Residues 1-254 of anthrax toxin lethal factor are sufficient to cause cellular uptake of fused polypeptides. J. Biol. Chem., **268**, 3334-3341.
 13. **GaneshKumar N., Arora N., and Kolenbrander P.E. (1993):** Saliva binding protein (SsaB) from *Streptococcus sanguis* 12 is a lipoprotein. J. Bact. **175**, 572-74.
 14. **Arora N., Min K., Costa J. J., Rhim J. and Metcalfe D.D. (1993):** Immobilization of bone marrow derived mast cells with Ad12-SV40 virus. Int. Arch. Allergy Appl. Immunol. **100**, 319-327.
 15. **Klimpel K.R., Arora N. and Leppla S.H. (1994):** Anthrax toxin lethal factor contains a zinc metalloprotease consensus sequence which is required for lethal toxin activity. Mol. Microb. **13**, 1013-1100.
 16. **Arora N., Williamson L.C., Leppla S.H., and Halpern J.L.. (1994):** Cytotoxic effects of a chimeric protein containing anthrax toxin lethal factor and tetanus toxin light chain in non-neuronal cell lines. J. Biol. Chem. **269**, 26165-26171.
 17. **Arora N. and Leppla S.H. (1994):** Fusions of anthrax toxin lethal factor with Shiga toxin

- and diphtheria toxin enzymatic domains are toxic to mammalian cells. *Infect. Immun.* **62**, 4955-4961.
18. Singh Y., Klimpel K.R., **Arora N.**, Sharma M. and Leppla S.H. (1994): The chymotrypsin sensitive Site, FFD³¹⁵, in anthrax toxin protective antigen is required for translocation of lethal factor. *J. Biol. Chem.* **269**, 29039-29046.
 19. Gordon V.M., Klimpel K.R., **Arora N.**, Henderson M.A. and Leppla S.H. (1995): Anthrax toxin protective antigen and diphtheria toxin, but not *Pseudomonas* exotoxin A, are proteolytically activated by both furin-dependent and independent pathways. *Infect. Immun.* **63**, 82-87.
 20. **Arora N.** (1996): Liposomes for allergy immunotherapy. *Ind. J. Allergy Appl. Immunol.* **10**, 61-64.
 21. Madan T., **Arora N.** and Sarma P.U. (1997): Identification and evaluation of a major cytotoxin of *Aspergillus fumigatus*. *Mol. Cell. Biochem.* **167**, 89-97.
 22. Goletz T.J., Klimpel K.R., **Arora N.**, Leppla S.H., Keith J.M. and Berzofsky J.A. (1997): Targeting of the MHC class I processing pathway with a novel gp-120 anthrax toxin fusion protein. *Proc. Natl. Acad. Sci (USA)* **94**, 12059-12064.
 23. Madan T., **Arora N.** and Sarma P.U. (1997): Ribonuclease activity of cytotoxin *Asp f1*, a major allergen from *Aspergillus fumigatus*. *Mol. Cell. Biochem.* **175**, 21-27.
 24. Masood R., Zheng T., Tulpule A., **Arora N.**, Chatlynne L., Hardy M., Whitmen Jr. J., Kaplan M., Dosik M., Ablashi D.V. and Gill P.S. (1997): Kaposi sarcoma-associated herpesvirus infection and multiple myeloma (Technical Comment). *Science* **278**, 1969-73.
 25. **Arora N.** (1997): Site directed mutagenesis of histidine residues in anthrax toxin lethal factor binding domain reduces toxicity. *Mol. Cell. Biochem.* **177**: 7-14.
 26. Sridhara S., **Arora N.** and Singh B.P. (1998): Stability of allergen extracts. *Ind. J. Allergy Appl. Immunol.* **12**, 1-4
 27. McGarvey M.E., Tulpule A., Cai J., Zheng T., Masood R., Espina B., **Arora N.**, Smith D.L. & Gill P.S. (1998): Emerging treatments for epidemic (AIDS-related) Kaposi's sarcoma. *Curr. Opin. Oncol.* **10**, 413-21.
 28. Thomas B., Sridhara S., Singh B.P. and **Arora N.** (1998): Role of cytokines in health and diseases. *Ind. J. Allergy Appl. Immunol.* **12**, 65-69.
 29. **Arora N.** and Gangal S.V. (1998): Liposome entrapped allergen reduces plasma histamine in sensitized mice. *Asian Pac. J. Allergy Immunol.* **16**, 87-91.
 30. **Arora N.**, Masood R., Zheng T., Cai J., Smith D.L. and Gill Parkash. (1999): Vascular endothelial growth factor chimeric toxin is highly active against endothelial cells. *Cancer Res.* **59**, 183-88.
 31. Masood R., McGarvey M.E., Zheng T., Cai J., **Arora N.**, Smith D.L., Sloane N. and Gill P.S. (1999): Antineoplastic urinary protein inhibits Kaposi's sarcoma and angiogenesis invitro and invivo. *Blood* **93**, 1038-44.

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35. Bisht V., Singh B.P., Gaur S.N., **Arora N.** and Sridhara S. (2000): Allergens of *Epicoccum nigrum* grown in different media for quality source material. Allergy (EJAAI) **55**, 274-280.
36. Verma J., Singh B.P., Gangal S.V., **Arora N.** and Sridhara S. (2000): Purification and partial characterization of a 67 kDa cross-reactive allergen of *Imperata cylindrica* pollen extract. Int. Arch. Allergy Immunol. **122**, 251-256.
37. Sharma M., Khanna H., **Arora N.** and Singh Y. (2000): Anthrax mediated delivery of cholera toxin A subunit into cytosol of mammalian cells. Biotechnol. Appl. Biochem. **32**, 69-72.
38. Kumar R., Sridhara S., Verma J., **Arora N.** and Singh B.P. (2000): Clinico-immunologic studies on allergy to pulses-a case report. Ind. J. Allergy Appl. Immunol. **14**, 15-20.
39. Bijli K.M., Singh B.P., Sridhara S. and **Arora N.** (2001): Isolation of total RNA from pollens. Prep. Biochem. Biotech. **31**, 155-162.
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41. Khanna H., Chopra A., **Arora N.** and Singh Y. (2001): Role of residues containing 2 β 1 strand of domain II in the biological activity of anthrax protective antigen. FEMS Microb. Lett. **199**: 27-31.
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47. Bisht V., Singh B.P., Kumar R., **Arora N.** and Sridhara S. (2002). Culture filtrate antigens and allergens of *Epicoccum nigrum* cultivated in semi-synthetic medium. *Med. Micro. Immunol.* **191**: 11-15.
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50. Bijli K.M., Singh B.P., Sridhara S., Gaur S.N. and **Arora N.** (2003) Effect of various stabilizing agents on *Imperata cylindrica* grass pollen allergen extract. *Clin. Exp. Allergy* **33**: 65-71.
51. Verma J., Singh B.P., Sridhara S. and **Arora N.** (2003) Purification and characterization of a 45 kDa major allergen of *Fusarium solani*. *Int. Arch. Allergy Immunol.* **130**: 193-199.
52. Bisht V., Kukerja N., Singh B. P., **Arora N.**, and Sridhara S (2003). Current status of fungal allergens. *Ind. J. Allergy Asthma Immunol.* **17**: 9-19.
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54. Goyal A., Kazim S.N., Sakhuja P., Malhotra V., **Arora N.** and Sarin S.K. (2004) Association of TNF- β polymorphism with disease severity among patients infected with Hepatitis C virus. *J. Med. Virol.* **72**: 80-5.
55. Bisht V., **Arora N.**, Singh B. P., Gaur S.N., and Sridhara S. (2004). Purification and characterization of a major cross-reactive allergen from *Epicoccum purpurascens*. *Int. Arch. Allergy Immunol.* **133**: 217-224.
56. Bisht V., **Arora N.**, Singh B.P., Pasha S., Gaur S.N., and Sridhara S (2004). EpiP 1, an allergenic glycoprotein of *Epicoccum purpurascens* is a serine protease. *FEMS Immunol. Med. Microbial.* **42**: 205-211.
57. Shanker J., Gupta P.D., Sridhara S., Singh B.P., Gaur S.N., and **Arora N.** (2005) Immunological analysis of cross-reactive glutathione-s-transferase allergen from fungal sources. *Immunol. Invest.* **34**: 37-51.
58. Kumari D., Kumar R., Sridhara S., **Arora N.**, Gaur S.N. and Singh B.P. (2005) Sensitization to blackgram allergy in patients of asthma and rhinitis: Clinical evaluation and characterization of allergens. *Allergy (In-press)*
59. Goyal A., Suneetha P.V., Kumar G.T., Sakhuja P., Shukla D.K., Arora N. and Sarin S.K. (2005) CCR5 Δ 32 mutation does not influence the susceptibility to HCV infection and severity of liver disease in chronic hepatitis C patients. *World J. Gastroenterology* (Accepted 2005)

Books chapters and proceedings

1. **Arora N.** and Gangal S.V.(1989): Potential use of liposomes in immunotherapy. New

Arora N.

Eng. Reg. Allergy Proc. 9, 627.

2. Leppla S.H., Klimpel K.R. and Arora N. (1993): Anthrax toxin receptor binding and internalization. In "Molecular Mechanisms of Bacterial Virulence", Kado CI and Crosa JH (eds.), 127-139.
3. Leppla S.H., Klimpel K.R. and Arora N. (1994): Development of anthrax toxin based fusion proteins for targeting of HIV infected cells. In "Bacterial Protein Toxins", F.J. Fehrenbach, and others (eds.), Suppl. 24, 431-442, Gustav Fischer Verlag, Stuttgart, New York.
4. Leppla S.H., Klimpel K.R. and Arora N. (1994): Anthrax toxin lethal factor is a metallopeptidase. In "Bacterial Protein Toxins", F.J. Fehrenbach, and others (eds.), Suppl. 24, 386-387, Gustav Fischer Verlag, Stuttgart, New York.
5. Leppla S.H., Klimpel K.R. and Arora N. (1994): Modified anthrax toxin is a potential anti-viral agent. In "Bacterial Protein Toxins", F.J. Fehrenbach, and others (eds.), Suppl. 24, 448-449, Gustav Fischer Verlag, Stuttgart, New York.
6. Leppla S.H., Klimpel K.R., Singh Y., Gordon V.M. and Arora N. (1996): Interaction of anthrax toxin with target cells. Salsbury Med. Bulletin 87, 91-92.
7. Gangal S.V., Arora N., Chugh L., Sehra S., Singh B.B., Malik B.K. (2000): Immunomodulation and immunotherapy using liposome entrapped allergens. In: regulatory control and standardization of allergenic extracts. Eds: R. Kurth and D. Haustein, Band 93; 9th International Paul-Ehrlich-Seminar, GIT VERLAG, GMBH, pg 267-74.
8. Singh B.P., Verma J., Arora N. and Sridhara S. (2000): Status of allergen standardization in India. In: regulatory control and standardization of allergenic extracts. Eds: R. Kurth and D. Haustein, Band 93; 9th International Paul-Ehrlich-Seminar, GIT VERLAG, GMBH, pg 41-45.
9. Singh B.P., Sridhara S. and Arora N. (2000): Quality control of allergen extracts. In: Ed. Rajendra Prasad, Advances in Allergy and Asthma, Shivam Publications, India, pg 101-105.
10. Arora N., Goyal A., Sridhara S. and Sarin S.K. (2003). Molecular testing in diagnosis and management of Hepatitis C virus. Mol. Probes in Laboratory Diagnosis pg 89-98.
11. Sridhara S., Shanker J., Arora N. and Singh B.P. (2003). Molecular probes in diagnosis of diseases. Mol. Probes in Laboratory Diagnosis pg 127-138.
12. Bijli K.M., Singh B.P., Sridhara S., Gaur S.N. and Arora N. (2003). Stability of *Imperata cylindrica* pollen allergens. Trends in clinical biochemistry and laboratory diagnosis. pg 309-313.
13. Bisht V., Singh B.P., Arora N. and Sridhara S. (2003). Epi n1₄₆₂₅ releases histamine in *Epicoccum nigrum* allergic patients and shows proteolytic activity. Trends in clinical biochemistry and laboratory diagnosis. pg 301-308.

Patents

1. Anthrax toxin related fusion proteins, nucleic acid encoding the same. US patent no. 5,591,631 dated 7th January 1997.

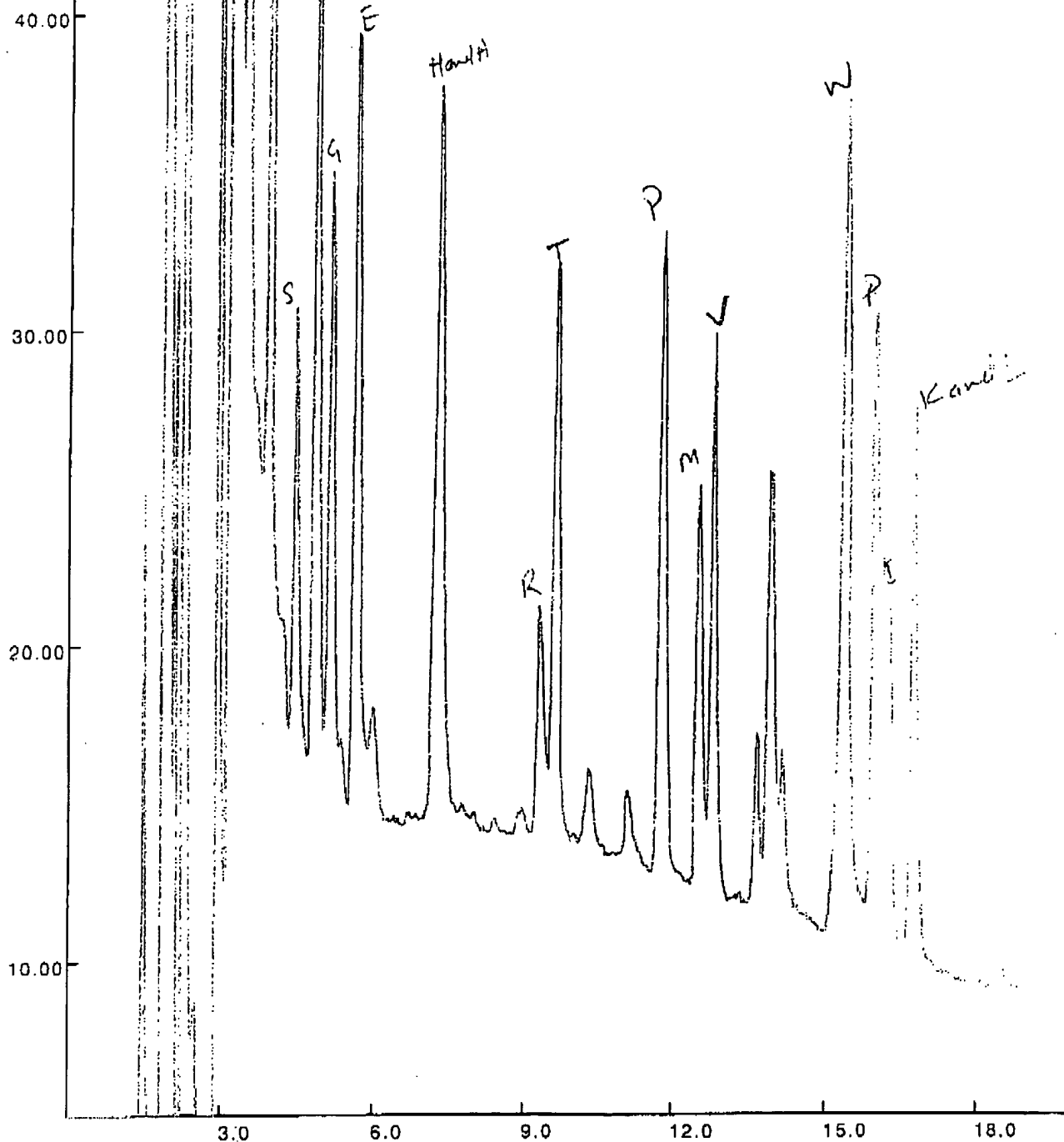
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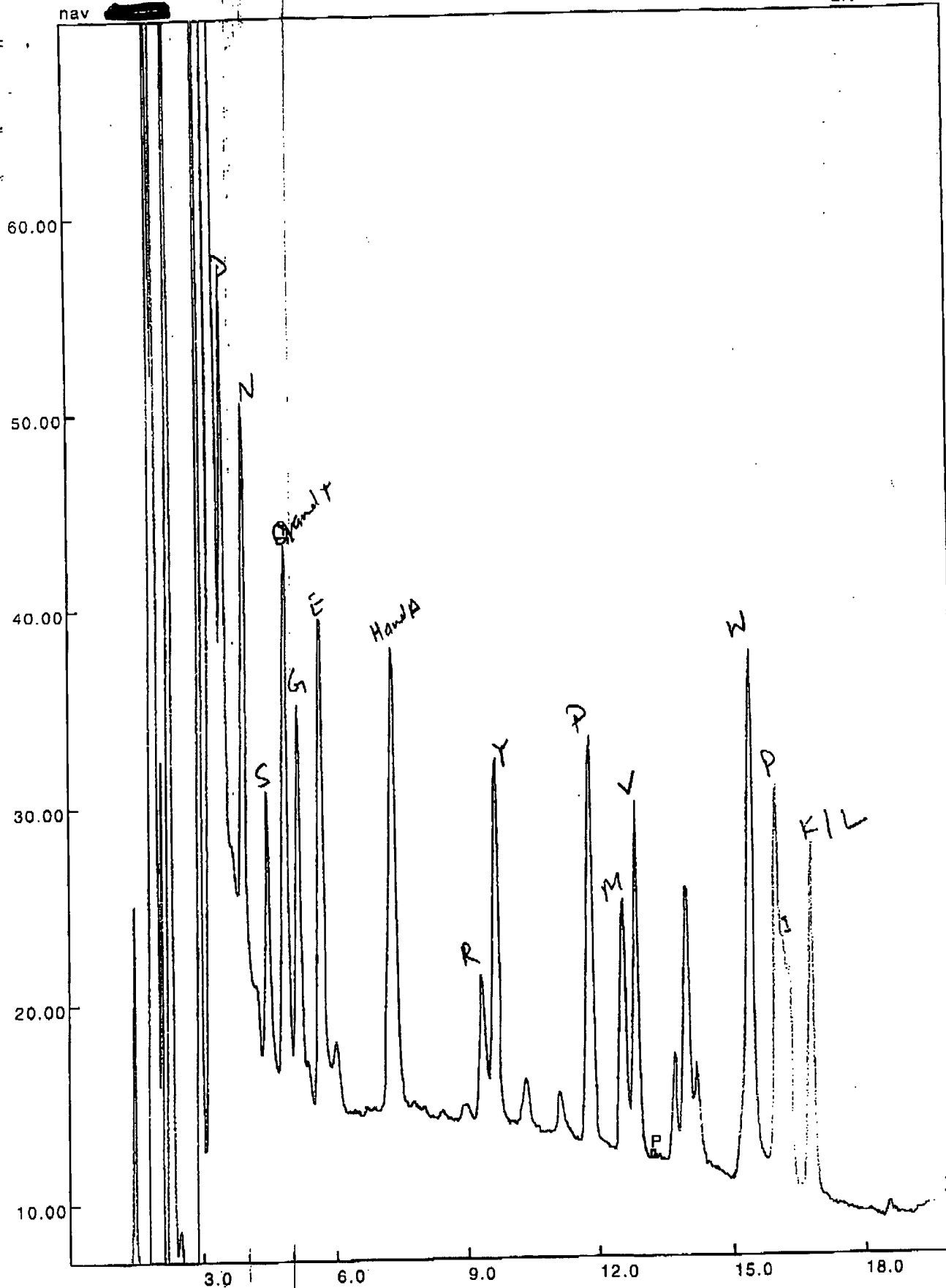
2. *Anthrax toxin fusion proteins and related methods. US patent no. 5,677,274 dated 7th October 1997.*
3. *Method of internalizing proteins into cells. European patent applied (February 1996).*
4. *Anthrax toxin fusion protein and related methods. Australian patent no. 682500, 1998*
5. *Targeting antigens to the MHC class I processing pathway with an anthrax toxin fusion protein. US patent no. 6,592,872 Oct 2003.*
6. *A novel protein capable of inhibiting anthrax toxin activity. US patent filed 19th Nov. 2003.*
7. *A novel protein capable of inhibiting anthrax toxin activity. PCT patent filed 27th Nov. 2003.*
8. *A novel protein capable of inhibiting anthrax toxin activity. Indian patent filed 20 Oct. 2004.*
9. *Formulation for the stabilization of allergenic extracts used for diagnosis and therapy of allergy. (Indian Patent filed, 330NF/05.*
10. *A Recombinant cross-reactive 12 kDa protein useful for detection of respiratory allergies. (Indian Patent filed, 162NF/05.*

Novel

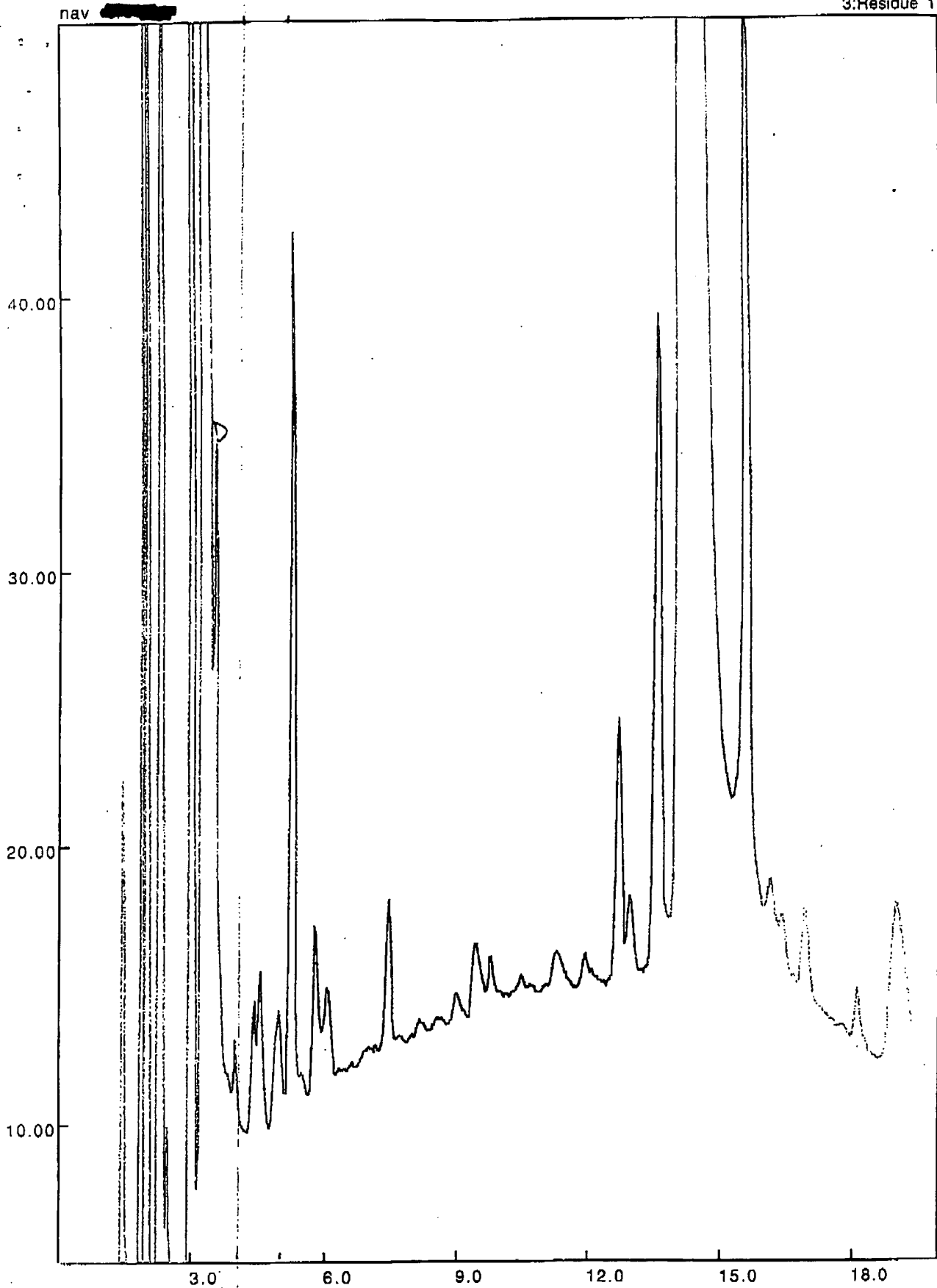
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2:Standard 1

Naveen Arora et al
US 10/715482Naveen



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4:Residue 2

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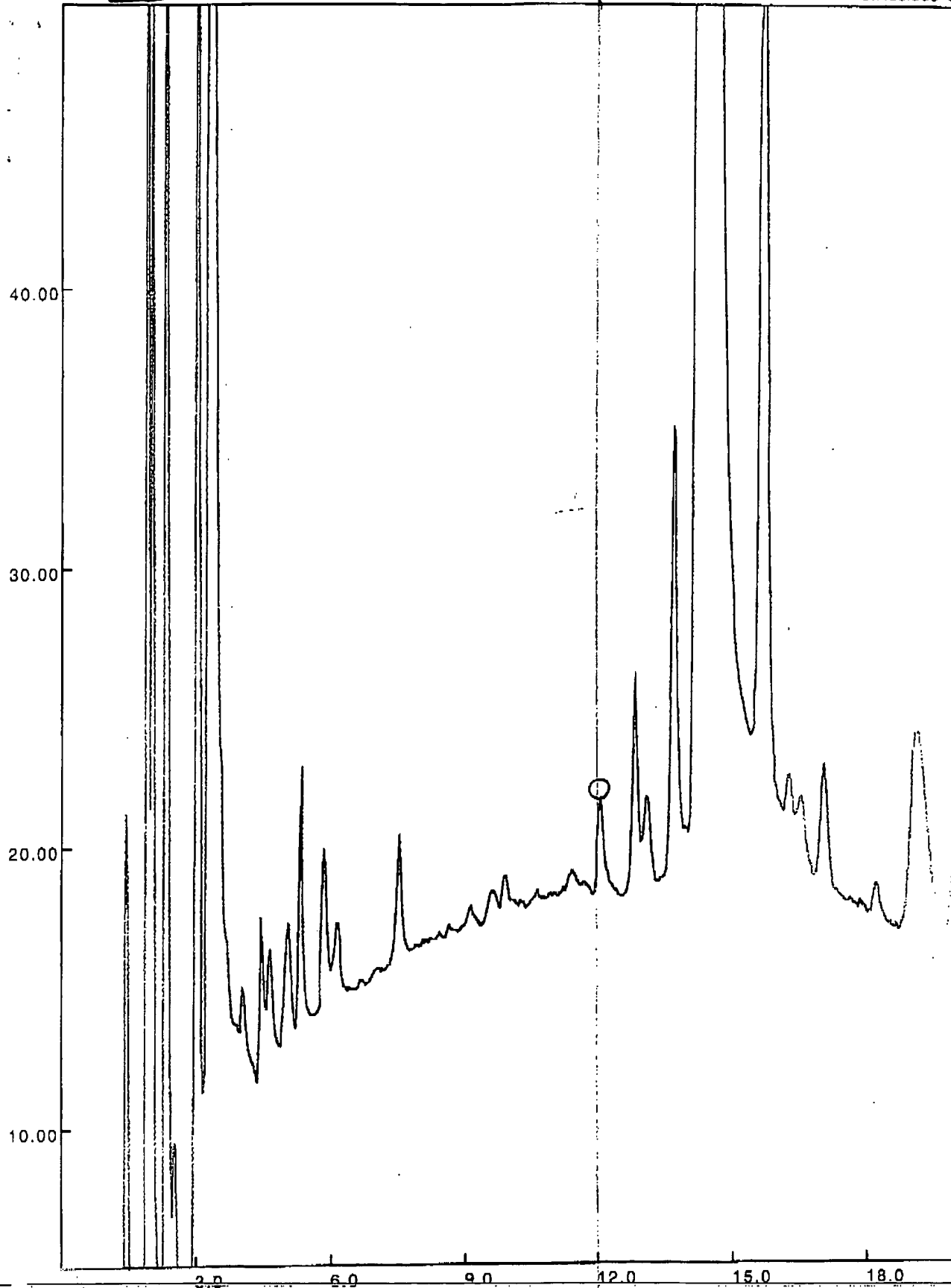
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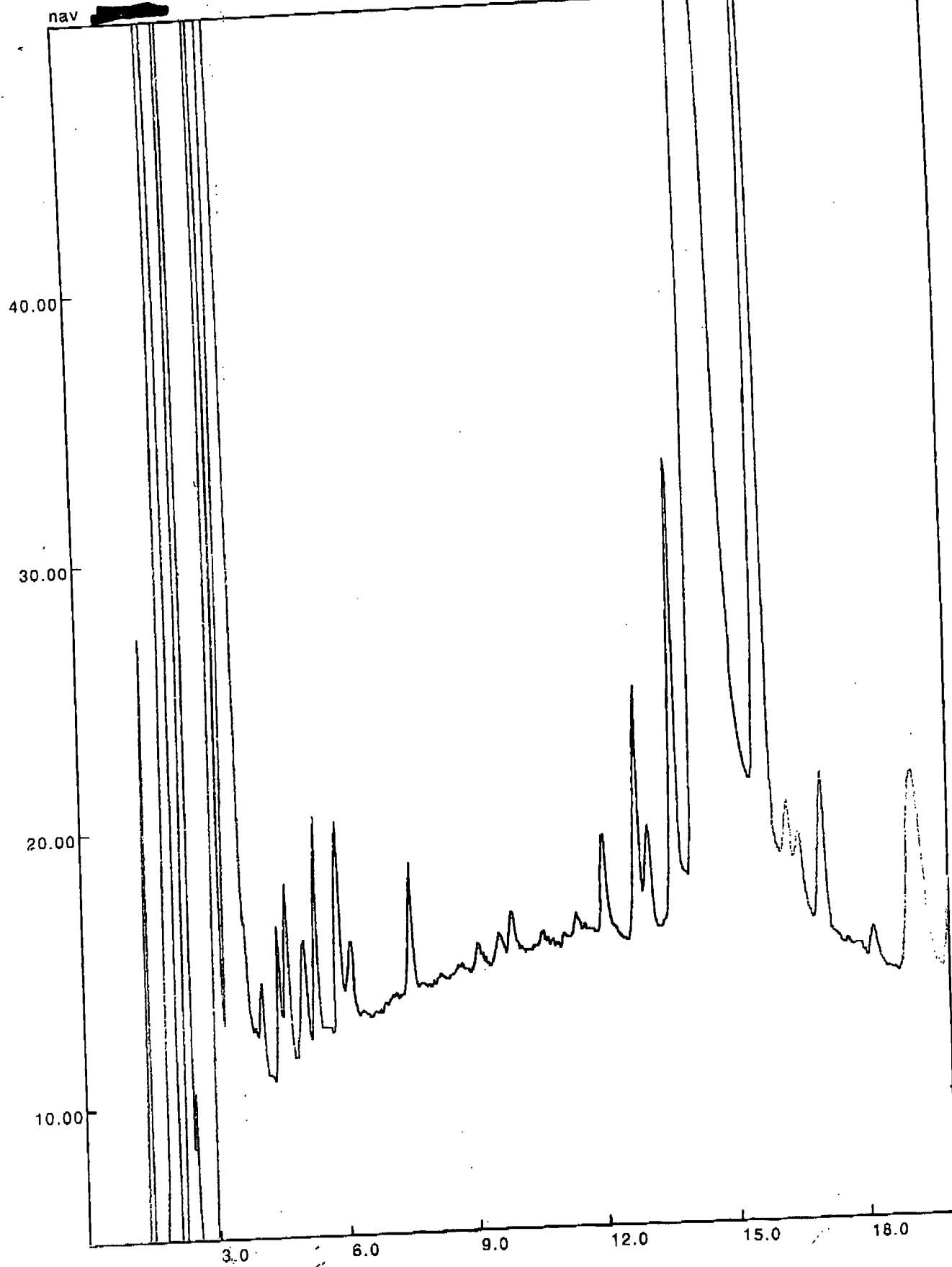
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5:Residue 3



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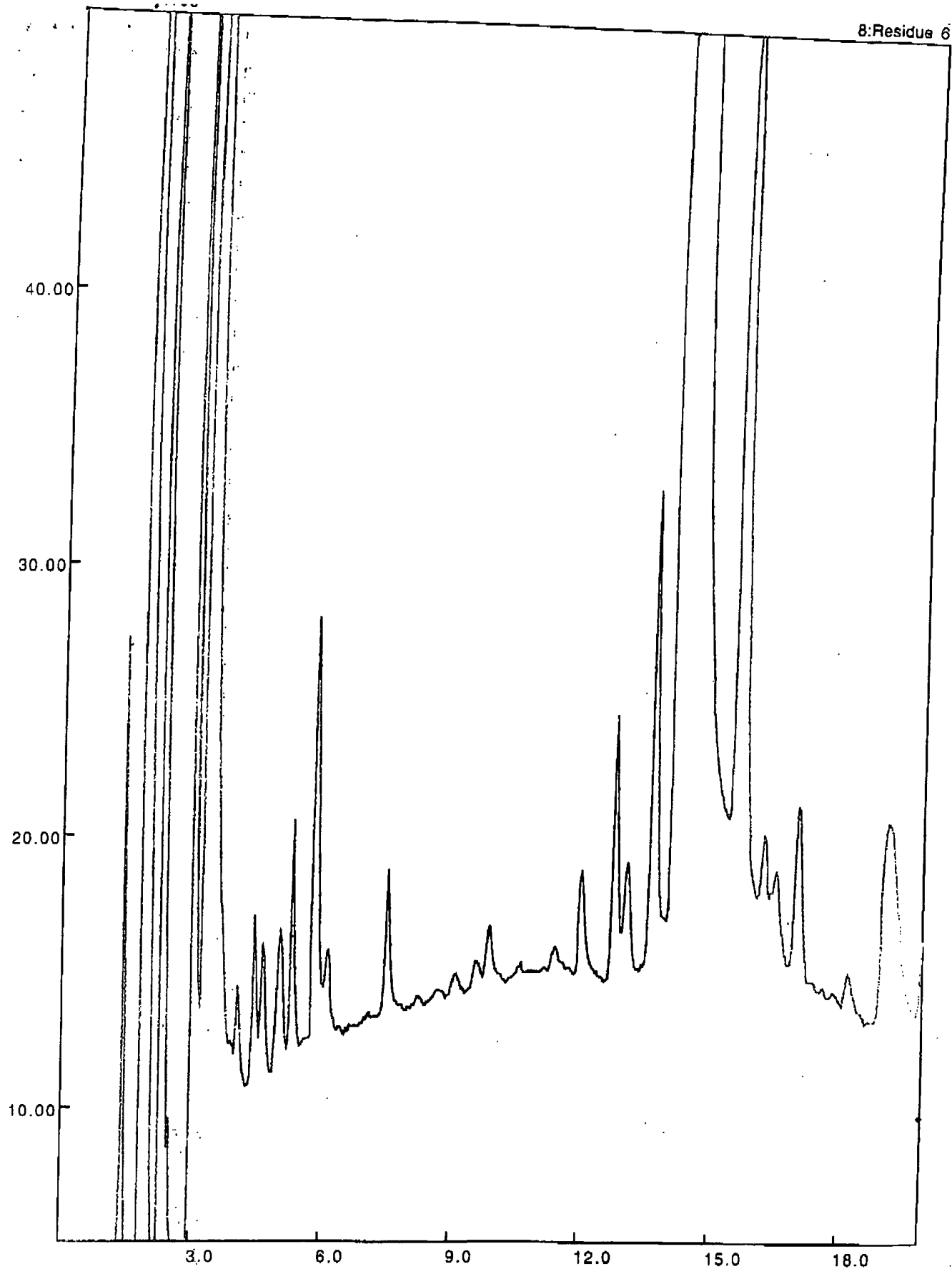
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Nov 2001

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Residue 1

Peak No	RT	Peak ID	Area	Pmol Area	BC
1	0.17		121157	0.80	0
2	1.11		17058	0.00	0
3	1.27		199492	4.86	1
4	1.48		35036221	9.56	3
5	1.91		84917293	10.73	3
6	2.00		20787030	0.00	3
7	2.33		32775478	11.19	3
8	2.49		1112639	6.74	3
9	2.69		911571	0.00	3
10	2.87		532572	0.27	3
11	3.00		20482912	10.35	3
12	3.28		112000864	6.26	3
13	3.53		8465150	9.85	3
14	4.01		1128673	2.03	2
15	4.42		1200070	3.21	1
16	4.57		1335257	3.58	3
17	4.99		1467569	0.00	3
18	5.25		7262593	18.56	3
19	5.46		188565	11.13	3
20	5.79		1957528	2.77	3
21	6.05		1231631	21.27	3
22	6.34		54060	0.00	3
23	6.42		22870	11.19	2
24	6.90		54173	0.00	1
25	6.97		35717	0.00	2
26	7.42		1401514	1.59	0
27	8.14		38216	0.00	0
28	8.61		1532	0.00	1
29	8.98		224873	12.59	2
30	9.43		1015590	0.00	1
31	9.77		375365	0.66	2
32	10.14		9020	0.00	0
33	10.46		143161	1.55	0
34	10.75		10770	0.00	0
35	11.03		14975	0.19	1
36	11.27		350442	4.37	2
37	11.91		276437	0.42	0
38	12.68		2932447	0.00	1
39	12.95		889627	1.57	2
40	13.55		8481852	0.00	1
41	14.08		49342882	0.00	3
42	14.38		532792119	0.00	3
43	15.55		18399543	17.66	3
44	16.12		1714379	2.00	3
45	16.41		759362	2.76	2
46	16.92		1106513	1.96	0
47	18.12		662659	0.00	0
48	19.01		123516	0.00	0

Residue 2

Peak No	RT	Peak ID	Area	Pmol Area	BC
1	0.71		5799	2.25	0
2	0.90		10792	0.00	0
3	1.23		168319	0.00	1

Novan

4	1.44	37095350	0.00	3
5	1.90	85518927	10.81	3
6	2.00	18294952	0.00	3
7	2.34	33342528	11.39	3
8	2.49	268797	1.63	3
9	2.66	756542	0.00	3
10	3.03	25959427	0.00	3
11	3.34	127556956	0.00	2
12	4.08	378134	0.68	0
13	4.44	1276986	3.42	1
14	4.64	1033105	0.00	3
15	5.06	3113943	0.00	3
16	5.31	3665724	0.00	3
17	5.61	61007	0.09	3
18	5.85	2000505	0.00	3
19	6.11	1111016	19.19	3
20	6.40	20627	10.10	2
21	6.69	36562	9.42	0
22	6.93	13381	0.00	0
23	7.49	1352817	1.53	0
24	8.01	42009	0.00	1
25	8.22	60855	53.43	2
26	8.60	57716	0.00	1
27	8.67	28276	0.00	2
28	9.08	329391	0.00	1
29	9.52	646464	0.00	3
30	9.85	527756	0.00	2
31	10.20	14439	0.16	0
32	10.57	216037	77.50	0
33	11.36	347104	0.00	0
34	12.00	866188	0.00	0
35	12.76	3002813	5.30	1
36	13.03	1200814	0.00	2
37	13.32	7795	0.00	1
38	13.62	6129015	38.89	2
39	14.16	53779399	307.66	1
40	14.45	500594260	156798.31	3
41	15.63	23825664	22.87	3
42	16.20	1698856	0.00	3
43	16.48	1433820	0.00	3
44	16.99	1751742	0.00	2
45	17.55	20302	0.00	0
46	17.88	4258	0.00	1
47	18.18	427976	0.00	2
48	19.06	7132858	0.00	0

Residue 3

Peak No	RT	Peak ID	Area	Pmol	Area	BC
1	0.16		29570		0.00	0
2	0.50		1189		0.00	0
3	1.20		5694		0.00	1
4	1.27		217578		5.30	3
5	1.48		35074046		9.57	3
6	1.92		80808278		10.21	3
7	2.01		17793595		0.00	3
8	2.35		31036403		10.60	3

Novex

10	2.69	787473	4.77	3
11	3.01	100435	0.00	3
12	3.33	21325422	10.77	3
13	3.90	100726253	0.00	2
14	4.07	44279	0.08	1
15	4.46	446376	0.80	2
16	4.64	1417264	3.80	1
17	5.05	1073085	0.00	3
18	5.32	1299878	0.00	3
19	5.86	2184652	0.00	2
20	6.13	1657795	0.00	1
21	6.65	1022751	17.66	2
22	7.29	13157	3.39	0
23	7.52	20883	0.02	1
24	8.07	1479318	1.67	2
25	8.64	18769	79.83	0
26	9.10	13589	0.00	0
27	9.59	210399	0.00	0
28	9.89	371120	0.65	1
29	10.50	235920	0.00	2
30	10.62	13140	0.00	0
31	11.21	10645	3.82	0
32	11.39	1527	0.02	1
33	11.72	23811	0.00	2
34	12.03	18705	0.03	1
35	12.40	959959	0.00	2
36	12.80	835	0.00	0
37	13.07	2533300	4.47	1
38	13.67	1093733	0.00	2
39	14.20	4889319	31.03	0
40	14.47	43799157	250.56	1
41	15.67	459655025	143975.14	3
42	16.23	20658729	0.00	3
43	16.51	1506418	5.47	3
44	17.02	1257561	0.00	3
45	17.90	1514955	0.00	2
46	18.21	1646	0.00	1
47	19.10	420766	0.00	2
		5460695	0.00	0

Residue 4

Peak No	RT	Peak ID	Area	Pmol Area	BC
1	0.25		9859	0.00	0
2	0.41		15275	0.00	0
3	0.73		26291	10.20	0
4	1.09		22407	0.00	1
5	1.23		207960	0.00	3
6	1.44		36574289	0.00	3
7	1.90		75168649	9.50	3
8	2.00		18084055	0.00	3
9	2.33		34014755	11.62	3
10	2.49		991149	6.01	3
11	2.66		563071	0.00	3
12	3.02		26977420	0.00	3
13	3.33		124568869	0.00	3
14	3.89		550967	0.99	3

Ames

12

		930723	1.00	1
15	4.07	1336985	3.58	3
16	4.44	936189	0.00	3
17	4.63	1366031	0.00	2
18	5.03	2173631	0.00	1
19	5.30	1984253	0.00	2
20	5.83	1010850	17.46	0
21	6.11	17678	8.65	0
22	6.43	5228	0.00	0
23	6.91	1275452	1.44	0
24	7.49	15283	1.55	0
25	7.80	196832	172.83	1
26	8.24	70278	3.93	2
27	9.05	81697	0.00	1
28	9.08	452969	0.80	2
29	9.54	552680	0.00	0
30	9.86	33206	0.00	0
31	10.54	6868	0.09	0
32	11.08	4730	0.00	1
33	11.33	17038	0.03	2
34	11.70	1427977	2.17	1
35	11.99	2946295	5.20	2
36	12.76	1238448	0.00	1
37	13.04	6601284	41.89	3
38	13.64	589675	1.28	3
39	13.89	52921873	302.75	3
40	14.16	485668042	152123.05	3
41	14.45	24795113	23.80	3
42	15.63	2035745	0.00	2
43	16.20	1007367	0.00	1
44	16.50	2383941	0.00	2
45	17.01	14296	0.00	0
46	17.33	10206	0.00	1
47	17.60	59156	0.00	2
48	17.86	421315	0.00	0
49	18.19	6506362	0.00	
50	19.09			

Residue 5 Peak No	RT	Peak ID	Area	Pmol Area	BC
1	0.18	109325	0.72		0
2	0.59	15860	9.24		0
3	1.02	14518	0.00		0
4	1.25	315097	7.68		1
5	1.47	35835487	9.78		3
6	1.92	70525150	8.92		3
7	2.01	17599466	0.00		3
8	2.35	34752861	11.87		3
9	2.52	949308	5.75		3
10	2.68	341265	0.00		3
11	3.03	26285536	0.00		3
12	3.34	119731077	0.00		3
13	3.90	596285	1.07		3
14	4.08	1028059	1.85		2
15	4.46	1318301	3.53		1
16	4.65	1616063	0.00		3
17	5.05	1274450	0.00		3

Notes

18	5.32	1881085	0.00	2
19	5.85	2044627	0.00	1
20	6.13	1023382	17.68	2
21	6.95	34767	0.00	1
22	7.11	51004	0.06	2
23	7.51	1250266	1.41	0
24	8.62	8413	0.00	0
25	9.10	119841	0.00	0
26	9.25	14644	0.05	1
27	9.56	11802	0.02	2
28	9.88	403062	0.00	0
29	10.56	77646	27.85	1
30	10.60	63652	22.83	2
31	10.84	23411	0.00	0
32	11.11	70618	0.88	1
33	11.37	177280	0.00	2
34	11.72	8457	0.01	1
35	12.02	1250465	0.00	2
36	12.78	2760296	4.88	1
37	13.06	1080895	0.00	3
38	13.66	5123701	32.51	2
39	14.19	47919522	274.13	1
40	14.46	474113025	148503.73	3
41	15.65	23016333	0.00	3
42	16.23	1844252	6.69	3
43	16.51	1300119	0.00	3
44	17.02	1936260	0.00	2
45	17.60	25959	0.00	0
46	17.92	2087	0.00	1
47	18.21	460805	0.00	2
48	19.12	2437617	0.00	1
49	19.16	3699417	7822.83	3
50	19.71	29914	12.65	2

Residue 6 Peak No	RT	Peak ID	Area	Pmol Area	BC
1	0.15	38286	0.00	0.00	1
2	0.26	59861	0.00	0.00	2
3	0.99	2560	0.00	0.00	0
4	1.46	38246069	10.44	10.44	1
5	1.92	84432569	10.67	10.67	3
6	2.00	20208634	0.00	0.00	3
7	2.36	34637398	11.83	11.83	3
8	2.52	1368611	8.30	8.30	3
9	2.68	537010	0.00	0.00	3
10	3.05	27253771	0.00	0.00	3
11	3.35	134095935	0.00	0.00	3
12	4.09	3441404	0.00	0.00	3
13	4.46	3882286	10.40	10.40	3
14	4.66	3167161	0.00	0.00	3
15	5.06	3541841	0.00	0.00	3
16	5.33	3424856	0.00	0.00	3
17	5.65	658466	0.93	0.93	3
18	5.85	4808400	0.00	0.00	3
19	6.13	1295791	22.38	22.38	2
20	7.09	19684	0.02	0.02	0

Ab/ean

21	7.52	1454995	1.65	0
22	7.81	8790	0.89	0
23	8.23	77302	67.87	0
24	8.66	16935	0.00	0
25	8.79	14701	0.00	0
26	9.10	141457	0.00	0
27	9.59	350673	0.62	1
28	9.89	570521	0.00	2
29	10.56	51929	18.63	1
30	10.62	57619	20.67	2
31	11.41	152519	0.00	0
32	11.72	1166	0.00	1
33	12.03	1179160	0.00	2
34	12.80	3079511	5.44	1
35	13.07	1367947	0.00	2
36	13.68	5328776	33.82	0
37	14.20	51309443	293.53	1
38	14.48	476718331	149319.78	3
39	15.67	21428471	0.00	3
40	16.25	606842	2.20	2
41	16.53	400021	0.00	0
42	17.04	2099840	0.00	0
43	17.38	19926	0.00	0
44	17.88	71829	0.00	1
45	18.23	542313	0.00	2
46	19.17	6247169	13210.34	0

Residue 7

Peak No	RT	Peak ID	Area	Pmol Area	BC
1	0.20		194666	0.00	1
2	0.31		90995	0.00	2
3	0.77		9903	0.00	0
4	1.44		38660029	0.00	1
5	1.90		83229614	10.52	3
6	2.00		19865353	0.00	3
7	2.35		34847829	11.90	2
8	2.67		673389	0.00	1
9	3.04		29968371	0.00	3
10	3.35		135295643	0.00	2
11	4.10		534245	0.00	1
12	4.45		1248363	3.34	3
13	4.67		812021	0.00	3
14	5.07		1542346	0.00	3
15	5.33		2130832	0.00	2
16	5.86		2994747	0.00	1
17	6.14		1156811	19.98	2
18	6.90		29841	0.00	0
19	7.10		64199	0.07	0
20	7.53		1562688	1.77	0
21	7.85		6115	0.00	1
22	8.10		19141	0.00	2
23	8.65		90776	0.00	1
24	8.77		48000	0.00	2
25	9.12		390082	0.00	0
26	9.61		302039	0.53	1
27	9.90		556544	0.00	2

Oxycen

		59123	21.21	1
28	10.59	115587	1.44	2
29	11.13	228510	0.00	0
30	11.42	1299662	0.00	1
31	12.04	3244322	5.73	2
32	12.80	1629373	0.00	0
33	13.09	5520731	35.03	1
34	13.69	57089073	326.59	3
35	14.21	506568107	0.00	3
36	14.50	26313820	0.00	3
37	15.68	1971617	7.15	3
38	16.26	3787479	0.00	2
39	16.55	2590989	0.00	0
40	17.05	521486	0.00	0
41	18.23	6065184	12825.51	
42	19.19			

Residue 8	RT	Peak ID	Area	Pmol	Area	BC
Peak No						
1	0.15	289425429		0.00		0
2	0.92	4488		0.00		1
3	1.38	1061		0.00		2
4	1.91	3987		0.00		1
5	2.20	3708		0.00		3
6	2.79	372		0.00		2
7	3.34	1248		0.00		1
8	4.05	8566		0.02		2
9	5.76	369		0.00		0
10	6.14	14228		0.25		0
11	7.71	1203		0.12		0
12	7.99	554		0.00		0
13	8.90	4236		0.00		0
14	9.82	598		0.00		0
15	10.43	7161		0.08		1
16	11.02	2377		0.03		3
17	11.12	394		0.00		2
18	11.72	457		0.00		0
19	12.25	630		0.00		1
20	12.41	1365		0.00		2
21	12.69	2815		0.00		0
22	14.00	294		0.00		0
23	14.50	9332		0.00		1
24	15.03	4640		0.00		3
25	15.31	588		0.00		2
26	15.62	977		0.00		0
27	16.20	250		0.00		1
28	16.43	805		0.00		2
29	16.62	3154		0.01		1
30	16.78	1517		0.00		2
31	17.32	206		0.00		0
32	17.89	308		0.00		1
33	18.13	1483		0.00		2
34	18.65	886		0.00		0
35	18.98	2569		0.00		0
36	19.53	213		0.00		0
37	19.77	196		0.00		0

Alou...

Residue 9

Peak No	RT	Peak ID	Area	Pmol	Area	BC
1	0.17		400379		0.00	0
2	0.47		458		0.00	1
3	0.60		108		0.06	2
4	1.14		150		0.00	0
5	1.69		1237		0.00	0
6	2.08		272		0.00	1
7	2.35		1378		0.00	3
8	2.47		457		0.00	2
9	2.77		1980		0.00	0
10	3.44		3630		0.00	1
11	3.53		5057		0.01	3
12	3.67		4387		0.00	2
13	4.08		1825		0.00	0
14	4.33		183		0.00	1
15	4.52		139		0.00	3
16	4.67		1534		0.00	3
17	4.86		1034		0.00	3
18	5.02		603		0.00	3
19	5.18		1004		0.00	2
20	5.88		2017		0.00	0
21	6.10		4681		0.08	1
22	6.23		3098		0.00	2
23	6.46		957		0.00	0
24	7.21		81		0.00	0
25	7.56		175		0.00	0
26	8.02		180		0.00	0
27	8.30		540		0.00	0
28	8.80		1770		0.00	0
29	9.21		2870		0.01	0
30	9.48		831		0.00	0
31	9.77		1173		0.00	0
32	9.94		113		0.00	0
33	10.98		114		0.00	0
34	11.39		1870		0.00	0
35	11.56		1135		0.00	0
36	11.80		98		0.00	1
37	11.95		108		0.00	3
38	12.10		1063		0.00	2
39	12.66		673		0.00	0
40	12.85		1075		0.00	1
41	12.95		2088		0.00	2
42	13.27		1772		0.00	0
43	14.13		2115		0.01	0
44	14.88		924		0.00	0
45	15.02		403		0.00	0
46	15.53		2205		0.00	0
47	15.84		2639		0.00	0
48	16.10		1369		0.00	0
49	16.69		3781		0.01	0
50	16.97		413		0.00	1
51	17.16		3401		0.00	2
52	17.42		1201		0.00	0
53	17.66		3412	24.74		1
54	17.89		4012	0.00		3

Nelson

16

55	18.07	1901	0.00	3
56	18.21	91	0.00	3
57	18.42	1618	0.00	2
58	18.61	1041	0.15	0
59	19.00	1496	0.00	0
60	19.58	1398	0.00	0

Residue 10	Peak No	RT	Peak ID	Area	Pmol	Area	BC
	1	0.69		2530		0.00	0
	2	1.05		2891		0.00	0
	3	2.00		2529		0.00	1
	4	2.20		1649		0.00	2
	5	2.84		1757		0.00	0
	6	3.15		1491		0.00	0
	7	3.58		2136		0.00	1
	8	3.66		2031		0.00	2
	9	4.91		3072		0.00	1
	10	5.07		1749		0.00	2
	11	5.30		726		0.00	0
	12	5.77		2203		0.00	0
	13	6.03		679		0.01	0
	14	6.85		1002		0.00	0
	15	7.48		88		0.00	0
	16	8.30		1092		0.00	0
	17	8.63		891		0.00	0
	18	9.39		2501		0.01	0
	19	9.87		3292		0.00	0
	20	11.98		1088		0.00	0
	21	13.21		770		0.00	0
	22	13.65		1688		0.01	0
	23	14.66		1826		0.00	0
	24	15.09		1507		0.00	0
	25	15.27		980		0.00	1
	26	15.43		3322		0.00	2
	27	15.75		1197		0.00	0
	28	16.16		706		0.00	0
	29	16.38		882		0.00	1
	30	16.52		1321		0.00	2
	31	16.91		2353		0.00	0
	32	17.32		2126		0.00	0
	33	18.69		1365		0.00	0
	34	18.95		1480		0.00	0
	35	19.66		898		0.38	0
	36	19.86		1236		0.00	0

Residue 11	Peak No	RT	Peak ID	Area	Pmol	Area	BC
	1	0.10		240056		0.00	0
	2	0.33		1238		0.00	1
	3	0.60		3724		2.17	2
	4	1.06		3332		0.00	0
	5	1.29		1852		0.05	0
	6	1.51		990		0.00	0
	7	1.80		2918		0.00	1

Alvarez

8	2.00	2206	0.00	4
9	2.28	6446	0.00	1
10	2.79	1922	0.00	3
11	2.90	2325	0.00	2
12	3.07	5213	0.00	1
13	3.38	2452	0.00	3
14	3.54	1322	0.00	2
15	3.70	2452	0.00	0
16	4.03	2054	0.18	1
17	4.26	1670	0.00	2
18	4.50	1418	0.00	0
19	4.88	1797	0.00	1
20	5.03	2666	0.01	2
21	5.21	1620	0.00	0
22	5.80	560	0.00	1
23	6.28	2321	1.14	3
24	6.43	883	0.00	2
25	6.58	980	0.00	0
26	7.06	2046	0.00	1
27	7.40	1549	0.00	2
28	7.52	4056	0.00	0
29	8.00	1269	0.09	0
30	8.43	2248	0.00	0
31	8.63	1062	0.00	1
32	9.37	1933	0.00	2
33	9.47	2138	0.00	0
34	10.01	1411	0.00	0
35	10.52	1772	0.00	0
36	10.75	1616	0.02	0
37	11.32	3966	0.01	1
38	11.83	6216	0.01	2
39	11.95	137	0.00	0
40	12.32	1609	0.00	1
41	12.65	1142	0.00	2
42	12.79	1670	0.00	0
43	13.07	1965	0.00	1
44	13.37	984	0.01	2
45	13.55	2112	0.00	0
46	14.37	1192	0.00	0
47	14.87	2083	0.00	0
48	15.59	1288	0.00	0
49	15.80	1168	0.00	0
50	16.15	1874	0.00	0
51	16.95	2328	0.00	0
52	17.26	1078	0.00	0
53	17.78	1378	2.91	0
54	19.20	1399	0.00	0
55	19.56	1011	0.00	0
56	19.88			

Name

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